INSTITUTE: National Cancer Institute

STUDY NUMBER: 04-C-0281 PRINCIPAL INVESTIGATOR: Steven Pavletic, M.D.

STUDY TITLE: Prospective Assessment of Clinical and Biological Factors Determining Outcomes in Patients with Chronic Graft-Versus-Host Disease

Latest IRB Review: Continuing Review 6/26/06
Latest Amendment Approved: Amend B 1/12/06
Standard

INTRODUCTION

We invite you to take part in a research study at the National Institutes of Health (NIH).

First, we want you to know that:

Taking part in NIH research is entirely voluntary.

You may choose not to take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled. However, to receive care at the NIH, you must be taking part in a study or be under evaluation for study participation.

You may receive no benefit from taking part. The research may give us knowledge that may help people in the future.

Second, some people have personal, religious or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). If you have such beliefs, please discuss them with your NIH doctors or research team before you agree to the study.

Now we will describe this research study. Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with anyone at NIH, or with family, friends or your personal physician or other health professional.

Purpose of the Study

You are being asked to participate in this study to allow us to advance our understanding of Chronic Graft versus Host Disease also known as cGVHD. You/your child may be eligible to participate in this study if you/your child have cGVHD or have signs or suspicion of having cGVHD.

cGVHD is one of the most serious side-effects and complications of blood or bone marrow stem cell transplant treatments. We know that cGVHD can affect just about any part of the body, especially the skin, mouth, liver, gut and eyes. This study will help us learn more about cGVHD. If we are able to better understand cGVHD, we may be able to develop better treatments for this disease in the future. We plan to evaluate 170 study participants over a five year period. This is a non-treatment study. We will not be testing any new treatments or medications. The main goal is to study the natural history of cGVHD while collecting clinical information from tests results and examinations we may do.

Your/your child's evaluation may also provide information indicating that you/your child are/is eligible for other studies at the NIH. If you are found eligible for other studies, there is no obligation to participate. Before you decide to take part in this study, please take as much time as you need to ask any questions and discuss this study with family, friends, your personal doctor or any NIH health professional.

DESCRIPTION OF THE STUDY

Baseline evaluation visit

You/your child should expect to make at least two separate 2-4 day visits to the NIH cGVHD clinic. You/your child will meet with members of the cGVHD Team, who will review your/your child's present and past medical history and determine whether you/your child have cGVHD. At a minimum, this study will require the collection of blood specimens and clinical data, which we will describe further in this consent.

The purpose of this baseline visit is to perform all clinical evaluations of your cGVHD and provide you with the multi-disciplinary team recommendations. These evaluations are standard of care we perform in all GVHD patients during their first clinic visit irrespective of participation on this study. At the same time, the clinical data containing information about your cGVHD are being stored at the time of the baseline evaluations and will be used for research analyses without revealing your identity.

THE FOLLOWING EVALUATIONS AND TESTS ARE DONE AT THE BASELINE EVALUATION VISIT EXCLUSIVELY FOR CLINICAL/MEDICAL PURPOSES AS STANDARD OF CARE PROCEDURES IN CGVHD PATIENTS: (the research part is that the data obtained about your cGVHD will be stored and used for analyses)

History and Physical Examination: A summary of your/your child's medical record will be requested from your/your child's physician when you/your child are initially referred to the NIH. In addition a physician or nurse practitioner will review your/your child's medical history with you/your child and you/your child will have a detailed physical examination. If you have had prior biopsies done, we may also ask your physician's office to send these samples for further diagnostic evaluations at the NIH.

Blood Tests: During your screening visits, blood will be drawn from a vein in your/your child's arm. About 2 tablespoons will be used for measurements of your/your child's blood counts, liver and kidney function, serum chemistries, and other routine tests.

Urine Tests: Includes a routine urinalysis and pregnancy test (adult female).

Pulmonary Function Test: Pulmonary Function Tests or PFTs measure the volume of air that a person can move into and out of the lungs in order to measure lung function. You/your child will breathe into a machine that measures the air **(routine pulmonary function tests are not done in children younger than 10 years of age).**

Bone Density Scan: This test measures the density of your bones (bone thickness). The scan checks for possible bone damage from your treatments. This scan will be recommended as routine care to be repeated at

12 months and then every two years. You/your child will not need to come to the NIH for the follow-up bone density scans. This is a non-research procedure and can be done through your primary doctor **(routine bone density scans are not done in children younger than 8 years of age).**

Biopsy of the affected organ to establish the diagnosis of cGVHD: Most commonly these organs are skin and/or oral (mouth) mucosa, less often but not uncommonly other organs such as liver, stomach or bowel. Organs such lungs or vagina can also require a biopsy if involved with manifestations that may represent cGVHD. The indication to perform a biopsy for diagnostic purposes is made by the treating physician-subspecialist and is based on the organ manifestation, clinical management need, and risk of performing a biopsy. If a clinical indication is made to perform a biopsy for diagnostic clinical purposes, the full procedure, medical reasons for doing it and all its risks and benefits will be explained to you by the treating physician who will perform the biopsy. Typically, for cGVHD diagnostic purposes at least one organ tissue biopsy must be obtained. If possible, a portion of such biopsy specimen obtained solely for a clinical indication will be used for research analyses.

Specialty Consultations: You/your child will also be evaluated by different specialists. Their evaluations will be helpful in deciding how to best manage your cGVHD. The specialty consultations are:

Nutritionist (Nutrition)
Physical Therapist (Rehabilitation)
Pain and Palliative Care Team (Pain and Comfort)
Ophthalmologist (Eye Specialist)
Social Worker
Gynecologist (Female Organ Specialist)
Dermatologist (Skin Specialist)
Dentist

Depending on your clinical symptoms other specialists that may be consulted include but are not limited to:

- Nephrologist (Kidney Specialist)
- Psychiatrist (Mental Health specialist)
- Neurologist (Nervous System Specialist)
- Hepatology/GI (Liver and Digestive Tract Specialist)
- Endocrinologist (Hormones, Glands Specialist)
- Pulmonologist (Lung specialist)
- Infectious disease
- Rheumatology (inflammatory or joint disease)

During the baseline evaluation visit other tests may be necessary to evaluate your cGVHD and provide you with best recommendations:

The procedures may include any of the following:

Imaging studies

- Chest X-ray
- Chest CT
- MRI
- Ultrasound
- Photographs, if you have skin involvement

Biopsies

- Tissue biopsy of an affected organ
- Tumor biopsy, if you/your child have a co-existing or recurrent cancer
- Bone marrow biopsy (if your blood counts are abnormal and need to be evaluated)

The indication to perform a biopsy for diagnostic purposes is made by the treating physician-subspecialist and is based on the organ manifestation, clinical management need, and the risk of performing the biopsy. Typically, for cGVHD diagnostic purposes at least one organ tissue biopsy must be obtained. If possible, a portion of such biopsy specimen obtained solely for a clinical indication will be used for research analyses.

Other possible interventions

- Upper and/or lower gastrointestinal endoscopy (if GI symptoms that may be due to cGVHD)
- Bronchoalveolar lavage (if lung symptoms that may be cGVHD or infection)

ALL NECESSARY CONSULTANTS AND SPECIALISTS WILL BE PROVIDED BY THE NIH CLINICAL CENTER. FOR PEDIATRIC PATIENTS THE CARE WILL BE PROVIDED BY THE NCI PEDIATRIC ONCOLOGY BRANCH TEAM AND THE NIH CLINICAL CENTER SPECIALISTS. IN CIRCUMSTANCES WHERE ADDITIONAL PEDIATRIC EXPERTISE WILL BE NEEDED, IT WILL BE PROVIDED THROUGH a CONTRACT WITH THE CHILDREN'S HOSPITAL MEDICAL CENTER.

Questionnaires

At the baseline visit we will also ask you to complete two sets of questionnaires.
1. **If 18 years of age or older** you will be asked to answer a specific questionnaire (called PG-SGA) about your nutritional habits. It will take about 30 minutes to complete the PG-SGA questions.
2. **If you/your child are older than 8 years of age** we also want to know about the effect that your/your child's illness has on behavior and everyday activities. These questionnaires are called the Quality of Life (QOL) Assessments. It will take about 60 minutes to complete QOL assessment questions.

THE FOLLOWING TESTS AND PROCEDURES ARE DONE FOR RESEARCH PURPOSES ONLY

1. Evaluations that will be used solely for research purposes and would be offered to all study participants include:

1. Collection and storage of routine clinical data
2. Analysis of samples of your diagnostic biopsy specimens
3. Extra blood obtained during the routine blood draws
4. Extra urine obtained during the routine urine sample collection

- The amount of blood that may be drawn from adults 18 years of age or older for research purposes will not be more than 1 pint every 6 weeks. For children under 18 years of age, the amount of blood drawn for research testing will be no more than 1/4 teaspoon per pound of body weight at one time and no more than 2/3 teaspoon per pound of body weight (maximum of 1 pint) every 6 weeks.

2. <u>The following research procedures will be offered to some participants:</u>

Collection of saliva (natural mouth fluid): This is a non-invasive procedure that will be performed in all participants who are 8 years or older.

Research Leukapheresis: You have option to decline this research procedure. **This procedure will be allowed ONLY in adult patients 18 years or older.**

Skin or Mouth Mucosa or Lip Biopsy: Includes up to two additional small samples of skin affected by cGVHD and two from a non-affected skin or mouth site. You have the option to decline these biopsies done for research purposes only. **These extra biopsies done only for research purposes will be allowed ONLY in adult patients 18 years or older.**

Tumor biopsy: In case of a co-existing malignant disease that is not in remission. **Such extra biopsy done only for research purposes will be allowed ONLY in adult patients 18 years or older.**

If you/your child have Scleroderma-type cGVHD (hardening of the skin) or Fascitis (inflammation of muscle sheets), the following non-invasive imaging procedures will be offered for research purposes only:

- **Research Ultrasound**
- **Research MRI (only if age 18 or above)** You have the option to decline the research MRI.

- Please circle and initial if you agree or disagree to having a research leukapheresis procedure.

I agree_____ I disagree_____

- Please circle and initial if you agree or disagree to having additional research skin or mouth mucosa biopsy procedure.

I agree_____ I disagree_____

- Please circle and initial if you agree or disagree to having additional tumor biopsy procedure only for research.

I agree_____ I disagree_____

- Please circle and initial if you agree or disagree to having a research MRI procedure.

I agree_____ I disagree_____

3. Follow-up research data collection

To complete the long term follow-up research part of this study, you/your child will **not** need to come back to the NIH. We will contact you/your child by mail and phone to complete the questionnaires and check on your health status. The Quality of Life Assessment (QOL) questionnaire will be completed yearly.

To complete the yearly QOL questionnaire a clinic visit is not necessary. We will mail you/your child the questionnaire. It takes approximately 15-20m minutes to complete the questionnaire.

We will also conduct a phone interview at months 6, 12, 18, 24, 30 and 36, and then yearly for up to 10 years. During the phone interview we will ask you general questions about your current health status. The phone interview takes about 20 to 30 minutes. If more information about you/your child's health is necessary, we may also contact your/your child's referring doctor.

SUMMARY RECOMMENDATIONS

At the end of the baseline multidisciplinary team evaluations in the NIH cGVHD clinic a summary of all of your/your child's clinical evaluations and treatment recommendations will be given to you/your child. We will also send a copy to your personal doctor.

RETURN VISIT

After completing baseline evaluations and receiving the multidisciplinary team recommendations **no follow-up appointments will be necessary at the NIH**. Our team will remain available to your primary physician as a resource for follow-up management questions or recommendations.

You/your child may be invited to return for follow-up evaluations at the NIH cGVHD clinic if:

- The original transplant was performed at the NIH
- You/your child are enrolling in another NIH research study, or
- Requested by the principal investigator.

At the time of your follow-up return to the NIH, our team will provide all standard of care evaluations and recommendations necessary for clinical management of your cGVHD.

At the time of a follow-up return we will ask you to allow us to perform one or more of the following non-invasive minimal risk studies for research purposes only:

- Obtaining a blood sample during a routine blood draw
- Obtaining a sample of a biopsy specimen performed for routine clinical diagnostic purposes
- Obtaining a non-invasive sample of saliva (if 8 years or older)
- Obtaining a research ultrasound

To perform the following research procedures you will need to sign a separate consent form at the time of return follow-up (these research procedures are NOT allowed in participants younger than 18 years of age):

- Obtaining an extra skin or oral mucosa biopsy for research only
- Leukapheresis

- Obtaining a research MRI

DESCRIPTION OF TESTS AND PROCEDURES:

- **Blood Draws**: In order to perform the routine laboratory tests, blood will be drawn from one of your/your child's arms with a needle. We would also like to draw the samples for research studies at this time.
- **Punch Skin Biopsy:** This is performed so that a piece of skin may be examined under the microscope to get a closer look at what is going on in your/your child's skin and for diagnostic purposes. After cleaning the skin with alcohol and/or another antiseptic, a local numbing medicine (Lidocaine with or without epinephrine)--similar to what a dentist injects to numb your gums--is injected into the planned biopsy site. A sharp instrument which looks like a miniature cookie-cutter is used to remove a round plug of skin about the size of a pencil eraser. The biopsy site may be left open or may be closed by putting in one or two stitches, and a small dressing is applied. Sometimes more than one such skin sample may be needed. You will be expected to keep the dressing over the biopsy site dry for 1 to 2 days. Thereafter, the dressing may be changed daily until the suture(s) are ready to come out, usually in 7 days. Depending on circumstances, the suture(s) may be removed by one of us, by your own doctor and/or your doctor's assistant.
- **Oral mucosa or lip biopsy:** The procedure is done in a similar manner as a skin biopsy, except that a dressing cannot be applied, because it is not possible to keep the area dry enough to keep the dressing on.
- **Collection of saliva (natural mouth fluid).** We will collect saliva from you after swabbing your tongue with a solution that tastes like lemon juice. We will collect the saliva that pools in your mouth, the saliva that collects under your tongue, and the saliva that comes into the mouth next to your upper back teeth. The techniques we use are non-invasive, and investigators at NIH have been collecting saliva with these methods for more than 20 years. We will give your saliva to Dr. Thomas Hart's laboratory (Human Craniofacial Genetics Section, NIDCR) for studies of proteins. We believe these studies will help us understand more about oral GVHD and lead to better treatments for this painful condition.
- **Urine Test:** You/your child will be asked to give a sample of your/your child's urine to be looked at under a microscope.
- **Pulmonary Function Test:** You/your child will be asked to breathe into a specialized machine that measures the air flow.
- **Completion of Composite Assessment Scales (CAS**): These are system specific medical evaluation summaries. They are completed by the specialist during your/your child's consultation. The results of these will be used to grade the severity/extent of your/your child's cGVHD.

The CAS consists of the following non-invasive tests consultations:

Ophthalmology Consultation (must be age 9 or older): Your/your child's eye evaluation will take place in the Eye Clinic and performed by an Ophthalmologist (eye specialist). Your/your child eye exam may take several hours to complete.

- **Measurement of Visual Acuity:** (the ability to see a vision chart) and eye pressure (measurement of fluid pressure in your eye). The doctor will look at your pupils and eye movements. The structures inside the eye will be examined through a special microscope. The lens and back of your eye will also be examined after drops have been placed in your eyes to dilate your pupils. The doctor also will look at your retina (inside your eye) with an ophthalmoscope (an instrument with a strong light and a magnifying lens).

- **Tear Tests:** Measurements of your tear production and function will be taken. The doctor will place anesthetic drops in your eyes and measure with special paper to measure how well your eyes produce tears.
- **Eye Surface Inflammation Measurements**: Drops of fluorescein and lissamine green (special eye dye) will be placed on the surface of your eye and on the inside of your lower eyelid. A slit lamp (special lamp to view the eye) will then be used to measure any inflammation on the surface of your eye and on the conjunctiva (membrane covering the surface of your eye and the inner eyelids).

Dermatology (Skin) Consultation: Your examination will be done in the Dermatology Clinic.
- Skin examination and evaluation
- Photos of your skin may be taken to record changes in skin disease**.**

Dental Consultation:
- Complete dental examination

Pain and Palliative Consultation (must be age 8 or older):
- Completion of the quality of life questionnaires
- Complete clinical evaluation by a Pain Specialist

Rehabilitation Consultation (must be age 4 or older):
- Clinical and physical examination
- Range of motion testing

Gynecology Consultation (must be age 16 or older):
- A complete examination of the female genitalia that include internal and external examination

Chest (CT) Scan:
- A computerized tomography or CT scan provides multiple pictures of inside the body. The CT scan may require the injection of dye (contrast) through a needle placed in your arm. CT scans can also be done with oral contrast. The scan takes between 30 and 90 minutes to complete depending on the areas of the body being scanned and the type of scanner. For this study the lungs and chest will be scanned.

Chest X- Ray:
- X-rays are single pictures taken of a body part by passing the x-rays through the body area. X-rays provide detail information about bones. Most x-rays take only a few minutes.

Ultrasound:
- Ultrasound uses harmless sound waves to provide pictures of organs or tissues inside the body. The sound waves bounce off the organs inside the body in a series of echoes that are recorded on a videotape.

MRI Scan
- MRI uses a strong magnetic field and radio waves to demonstrate structural and chemical changes in tissue.

Leukapheresis:

- This procedure is done in the Department of Transfusion Medicine (Blood Bank) and is supervised by the Blood Bank doctors. With this procedure we are able to collect a large number of white blood cells for research purposes. This procedure takes about 1-2 hours. The collected white blood cells will be analyzed in research laboratories and may be stored.
    - We may need to place one or two intravenous lines in your/your child's arm, or to have a single, larger intravenous line placed in a vein in your/your child's groin.
    - We will draw your/your child's blood into an apheresis (cell separator) machine, which will separate the white blood cells from the red blood cells and plasma through a spinning process.
    - The white blood cells will be collected into a bag, and the red blood cells and plasma will be returned to you/your child.
    - The collected white blood cells will be analyzed and may be stored.

Potential and Benefits Risks of Participation:

The primary benefit of this study is informative, not treatment. Your/your child's participation in this study will allow us to learn more about cGVHD. Based on our past experience in the NCI Multi-specialty Chronic Graft versus Host Clinic, so far, the likelihood is high that the possible medical, physical, social, and psychological benefits by being enrolled in this study significantly outweigh the risks of participating in this study for you/your child.

The planned research studies will have no direct clinical value to you/your child. We will not give you/your child the results of the research studies because we cannot interpret such results accurately enough for clinical care. If we develop meaningful information from this study that may be important to your/your child's health, we will inform you/your child of any useful results when they become available.

Expected direct benefits to you/your child include:

- A complete multi-specialty evaluation by experienced health professionals in the NCI.
- Availability to medical advice and consideration for any other potential studies.
- In case of any unexpected medical complications during the screening evaluation all necessary medical intervention and or recommendations will be provided by the study team.
- The cGVHD clinic staff will remain available as a long-distance consultation resource to you/your child's referring doctor.

RISKS OR DISCOMFORTS OF PROCEDURES:

Blood Draw: You/your child may experience:

- Mild pain or bruising at the site on your/your child's arm.
- There is a small possibility of fainting and infection.
- Similarly, there is a small risk of bleeding, blockage, or inflammation (infection) of the vessel
- Discomfort generally does not last long and permanent damage is extremely rare.

Skin Punch Biopsies: Whenever possible, we will perform biopsies on covered areas of the body.

- There may be minor bleeding right after the procedure and this can easily be controlled by applying pressure on the spot for a few minutes.

- Rarely, a bruise might form and this eventually goes away on its own.
- Sometimes a small infection may occur at the biopsy site. This can usually be treated with topical antibiotics.
- On the very rare occasion that a larger or deeper infection occurs, oral antibiotics may be needed for 7-10 days. An infection can be recognized by redness, soreness, and pus at the site. It generally starts 2 days or more after the procedure and does not clear up in another couple of days. These biopsy/excision sites generally heal very well, leaving red, white, dark or skin-colored flat scars.
- Sometimes, the scar that forms may be a bit thicker than usual. Rarely, a keloid (large, painful or itchy scar) may form. Keloids are more likely to form on the chin, earlobes, chest and upper backs of Blacks and Asians between adolescence and the 30's.

Oral mucosa or lip biopsy: There may be minor bleeding.

- Bruising and slight swelling
- Possibility of infection
- Numbness
- Mouth sores have occurred in some patients, but this is uncommon

Photography: Only photos of your affected skin will be taken.

- You/your child will not be recognizable from the photos

Pulmonary Function Test: These tests are safe and side effects are unlikely.

- During the test you may be asked to breathe deeply or rapidly which may occasionally cause brief lightheadedness or slight soreness of the chest

Eye Examination: You/your child may experience:

- Blurry vision
- Sensitivity to light. This is only temporary and completely reversible. You will be given a pair of sunglasses to protect your eyes from the light.

Leukapheresis Procedure:

- You/your child may experience numbness or tingling around the lips or fingertips. This is due to the blood thinner that is given during the procedure. This is easily treated by slowing down the procedure and giving calcium supplements.
- Blood infections from contamination of the apheresis machine are a remote possibility.
- On rare occasions, allergic reactions may occur during apheresis, or a participant may lose as much as a unit of blood due to machine malfunctions. We treat these events by stopping the procedure and giving antihistamines or intravenous salt solutions.
- We will make all attempts, including additional blood and platelet transfusions if needed, to protect you/your child from any complications of apheresis.

Imaging, Scans and Radiology Tests: (MRI, CT, Ultrasound and X-rays)

This research study involves minimal exposure to radiation to be given only in circumstances required for medical diagnostics and not research reasons. The amount of radiation to be used in this study is within the dose guidelines

established by the NIH Radiation Safety Committee for Research Subjects. If you would like more information about radiation and examples of exposure levels, An Introduction to Radiation for NIH Research Subjects is available. Please ask the study investigator or nurse for a copy of the pamphlet.

- The most common discomfort is the length of time a patient must lay still or flat while the scan or the x-ray is being preformed.
- Occasionally a patient may become uncomfortable within the closed spaced of the scanners. If this occurs cool air can be blown over you/your child by a fan if desired or the doctor can order a medication to help you/your child relax.
- If a contrast agent (special dye) is ordered with the scan there is a small risk of having a reaction to the contrast. In a small group of patients who have a reaction, the most common symptom is nausea, pain in the vein where the contrast was given, headache, a metallic bitter taste in the month and a warm or flushing feeling that lasts 1-3 minutes. Rarely, these symptoms may require treatment.
- In very rare cases people have had more severe allergic reactions that result in shortness of breath, wheezing, or lowering of the blood pressure. If you/your child had a reaction in the past, be sure to tell your doctor or nurse about it. Also, the amount of radiation (dye) dose is within safe limits as defined by the NIH Radiation Safety Guidelines
- Individuals with fear of confined spaces may become anxious during MRI.
- You/your child will lie on a table in a space enclosed by a metal cylinder (the scanner itself). You/your child may need to stay within the cylinder for 1-2 hours.
- You/your child will be asked to lie very still for 10 to 15 minutes at a time.
- Patients are at risk for injury from MRI if they have metal objects in their bodies, such as pacemakers, aneurysm clips (metal clips on the wall of a large artery), metallic prostheses, cochlear implants, or shrapnel fragments. Welders and metal workers are also at risk for eye injury because of unsuspected tiny metal fragments there.
- You/your child will hear a thumping noise created by the radio waves forming the images.
- You/your child will feel no pain, but you/your child may find the noise and the closed-in space discomforting.
- The MRI operators will observe you/your child at all times, and you/your child will be able to speak to them; you/your child can ask to be moved out of the machine at any time.

Unforeseeable and/or unknown risks/discomforts may occur

Research Subject's Rights:

Your/your child's participation in this study is voluntary. You/your child have the right to discontinue participation in this study at any time.

- You/your child will be given a copy of this consent for your/your child's records
- You/your child are encouraged to ask questions of the staff, your primary doctor and or family members
- There will be no charge to you/your child for any of the cost that are directly related to this study
- You/your child have/has the right to refuse any tests or procedures in this study

Alternative Approaches or Treatments:

Other alternatives which can be considered for you/your child include:

- Seek regular medical care in a GVHD clinic
- Seek regular medical care with your physician

Compensation:

There is no compensation for your/your child's participation in this study.

OTHER PERTINENT INFORMATION

1. Confidentiality. When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

The Federal Privacy Act protects the confidentiality of your NIH medical records. However, you should know that the Act allows release of some information from your medical record without your permission, for example, if it is required by the Food and Drug Administration (FDA), members of Congress, law enforcement officials, or other authorized people.

2. Policy Regarding Research-Related Injuries. The Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the National Institutes of Health, the Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

3. Payments. The amount of payment to research volunteers is guided by the National Institutes of Health policies. In general, patients are not paid for taking part in research studies at the National Institutes of Health.

4. Problems or Questions If you have/your child has any problems or questions about this study, or about your/your child's rights as a research participant, or about any research-related injury, contact the Principal Investigator, Dr Steven Pavletic; Building 10, Room 4-3130, Telephone: 301-402-4899. Other researcher you may call is: Dr Alan Wayne, Building 10, Room 1W3742, Telephone 301-496-4256.

You may also call the Clinical Center Patient Representative at (301) 496-2626.

5. Consent Document. Please keep a copy of this document in case you want to read it again.

COMPLETE APPROPRIATE ITEM(S) BELOW:

A. Adult Patient's Consent

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby consent to take part in this study.

Signature of Adult Patient/Legal Representative _____ Date _____

B. Parent's Permission for Minor Patient.

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby give permission for my child to take part in this study. (Attach NIH 2514-2, Minor's Assent, if applicable.)

Signature of Parent(s)/Guardian _____ Date _____

C. Child's Verbal Assent (If Applicable)

The information in the above consent was described to my child and my child agrees to participate in the study.

Signature of Parent(s)/Guardian _____ Date _____

THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE FROM JUNE 26, 2006 THROUGH JUNE 25, 2007.

Signature of Investigator _____ Date _____ Signature of Witness _____ Date _____